e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(6); 2276-2283

Original Research Article

Comparison of Clinical Effectiveness of Propofol as A Standalone Agent Versus the Combination of Propofol and Ketamine for Ambulatory Anaesthesia: A Clinical Study

Soumyakanta Sethi[1], Alok Kumar Sahoo[2], Chittaranjan Panigrahi[3]

[1]Assistant Professor, Department of Anaesthesiology, SCB Medical College, Cuttack, Odisha, India

[2]Assistant Professor, Department of Anaesthesiology, SCB Medical College, Cuttack, Odisha, India

[3]Associate Professor, Department of Anaesthesiology, DD Medical College, Keonjhar, Odisha, India

Received: 21-04-2023 / Revised: 22-05-2023 / Accepted: 26-06-2023

Corresponding author: Dr Soumyakanta Sethi

Conflict of interest: Nil

Abstract:

Propofol's solubility, rapid induction, and short recovery time, as well as its amnestic and antiepileptic properties, make it a potent anaesthetic agent that has acquired a great deal of popularity and is widely used in elective surgeries. Hypotension, respiratory depression, wheezing, hiccups, laryngospasm, and movement may be dose-dependent side effects of the exclusive use of propofol for LMA administration. Studies revealed that a combination of ketamine and propofol decreased patients' use of propofol and opioids and enhanced their hemodynamic and respiratory stability. Our study's primary objective was to compare the clinical efficacy of propofol alone versus propofol and ketamine during ambulatory anaesthesia. This hospital-based randomised double-blind investigation was conducted with 80 patients in the department of anaesthesiology at SCB Medical College, Cuttack over a two-year period. Patients belonging to ASA I & II, aged between 20 and 40 years, were sampled in groups of 40. Group P: Only Propofol Combination of propofol and ketamine in Group PK. The doses of induction, pulse rate, oxygen saturation, systolic, diastolic blood pressure, mean arterial pressure, and complications, if any, were recorded. T test analysis revealed statistically significant differences between induction dose, systolic, diastolic, mean arterial pressure, and complications.

Keywords: LMA, ASA.

Introduction

Propofol is familiar as an effective anaesthetic and analgesic agent in a variety of elective procedures due to its rapid onset and recovery, as well as the fact that it has fewer unwanted side effects than its homologues [1, 2]. Though limited cardiorespiratory depressant effects, therapeutic index, and a lack of analgesic properties hinder its effectiveness as a dynamic anaesthetic agent [1-3], there is no single medication that satisfies the aforementioned criteria, so anaesthesiologists use a mixture of drugs in standardised doses to achieve maximum efficacy [4]. Propofol is co-administered with other anaesthetic agents with excellent analgesic activities, such as ketamine, fentanyl, or sevoflurane, to mitigate these

limitations. Nonetheless, the search for a suitable co-induction agent for propofol is a constant and active area of medical research. In the context of general anaesthesia, ketamine (an antagonist of NMDA receptors) and fentanyl (a potent lipid-soluble opioid) have emerged as effective co-induction agents used in conjunction with propofol [5,6].Due to its hemodynamic property, propofol (2, 6-di-isopropyl phenol) is the most recently introduced intravenous anaesthetic and is currently in widespread use. Propofol is a non-opioid, non-barbiturate hypnotic sedative. It has an antiemetic effect and consistently induces sedation. Because of its clear-headed recovery, it is preferred in outpatient surgical procedures. Depression of the cardiovascular and respiratory systems, bradycardia, and hypotension are dose-related adverse effects. It lacks analgesic properties as well.

Ketamine is very dissimilar to propofol. It generates a distinct type of anaesthesia known as "dissociative anaesthesia" as well as analgesia. It has a sympathomimetic effect and retains spontaneous ventilation, both of which are advantageous for procedural sedation [2]. It can cause psychomimetic adverse effects, such as emergence agitation and vivid dreams [3,4].Theoretically, the combination of ketamine and propofol (ketofol) should have the benefits of both medications and complement each other's drawbacks. Ketamine's sympathomimetic effect may compensate for the propofol-induced deterioration in hematologic function. It is known that coadministration of propofol reduces psychomimetic adverse effects [7, 8]. Indeed, the combination has been shown to be beneficial in a variety of clinical situations, with improved profiles of respiratory depression, analgesia, hemodynamic stability, and outcomes compared to each agent alone. The efficacy of the combination of ketamine and propofol for PSA is the subject of ongoing debate [9]. Although ketamine and propofol theoretically have synergistic efficacy and counterbalance each other's drawbacks, it is unknown if this translates to enhanced patient outcomes. Since the publication of previous reviews on this topic [10], new evidence from clinical trials has become available. Propofol alone will be compared to propofol and ketamine for TIVA in ambulatory anaesthesia.

Methodology

The present study was conducted in the department of anaesthesiology at SCB Medical College, Cuttack, India. After obtaining institutional ethical committee approval and patients' written informed consent, the study was conducted on 80 patients, aged 20 to 40 years, of ASA grade I and ASA grade II, who were scheduled for ambulatory anaesthesia, such as incision and drainage of abscesses and closed reduction of fracture upper limb.

Patients were randomly assigned to one of two groups (40 in each), receiving either propofol alone (Group P) or a combination of propofol and ketamine (Group PK), and the following variables were recorded:

- Haemodynamics, intra operatively.
- Induction requiremts, of propofol and ketamine.
- Time of recovery from induction.
- Incidence of post-operative Complications.
- Duration of pain relief post operatively.

Patients with ASA grades III, IV, and V, patients under 20 years of age and over 40 years of age, recalcitrant patients, and patients with a history of drug allergy were excluded from the study. Randomization and double blindness served as the selection method. All patients fasted for at least six hours prior to undergoing anaesthesia. The preoperative baseline values for heart rate, blood pressure, and SpO2 were recorded.

Intra Operative Period

After securing 18 G cannula and connecting to NIBP, pulse oximeter and ECG monitor,

patients were premeditated 15 to 20 minutes prior to induction with

- Injection Glycopyrulate 0.2mg.
- Injection ondansetron 4mg.
- Injection fentanyl 1microgram per kg.
- Injection midazolam 1mg.

The anaesthesia machine, oxygen delivery system, emergency resuscitation apparatus, and emergency drugs were kept on hand. In a double-blind fashion, participants were randomly assigned to one of the two groups, viz-a-viz:

- Group P: 40 pt. received propofol slowly till the point of induction.
- Group PK: 40 pt. received ketamine 0.5mg per kg IV slowly followed by propofol IV till the point of induction.

Baseline Blood Pressure, Pulse rate, respiratory rate, SpO_2 were recorded.The anaesthesia was then maintained with propofol bolus 10mg IV in the propofol group and with propofol ketamine bolus 10+10mg IV in the propofol-ketamine group based on requirements, including spontaneous moments, tachycardia, elevated blood pressure, an increase in respiratory rate, and the appearance of tears. Maintaining spontaneous respiration with 100% O2 using a respirator and bain's circuit. Blood Pressure, ECG Changes, Respiratory rate, basal Pulse Rate, and Saturation were recorded every 5 minutes until the end of the procedure, followed by a recording every 5 minutes. The duration of postoperative pain relief was also recorded. For nausea and vomiting, 100-150 microgram per kilogramme of IV ondansetron was administered. The time of the first analgesic request was recorded. The patient received regular analgesics for the remaining 24 hours to alleviate discomfort.

- Hypertension defined as >140/90 mm of hg
- Hypotension defined as < 90/50 mm of hg
- Hypoventilation defined as respiratory rate <8/minute
- Desaturation defined as SPO2 <93%

All the parameters were monitored very keenly.

Statistical Analysis

The Student T-Test was used to assess the statistical significance of paired date a p value of <0.05 was considered significant.

Results

Of the 125 patients deemed eligible, 45 refused to participate and were therefore excluded. None of the eighty randomised patients were excluded from the analysis. The demographic profiles of the scheduled patients for the investigation were comparable.

Table 1: Intergroup comparison of changes in systolic blood pressure

Mean Systolic BP	Propofol		Propofol-Ketamine		T stat	P - Value	Inference
	Mean	SD	Mean	SD			
At 0 MIN	118.4	9.36	117.9	8.77	0.22	>0.05	NS
At 5 MIN	96.3	7.35	120.6	8.28	-13.89	<0.001	HS
At 10 MIN	99.7	6.68	122.9	8.14	-13.96	<0.001	HS
At 15 MIN	103.8	7.03	117.9	7.99	-8.43	<0.001	HS
At 20 MIN	108.9	5.64	123.3	7.93	-9.33	<0.001	HS
At 25 MIN	110.1	5.35	121.4	7.95	-7.46	<0.001	HS
At 30 MIN	110.9	5.45	122.6	6.99	-8.31	<0.001	HS

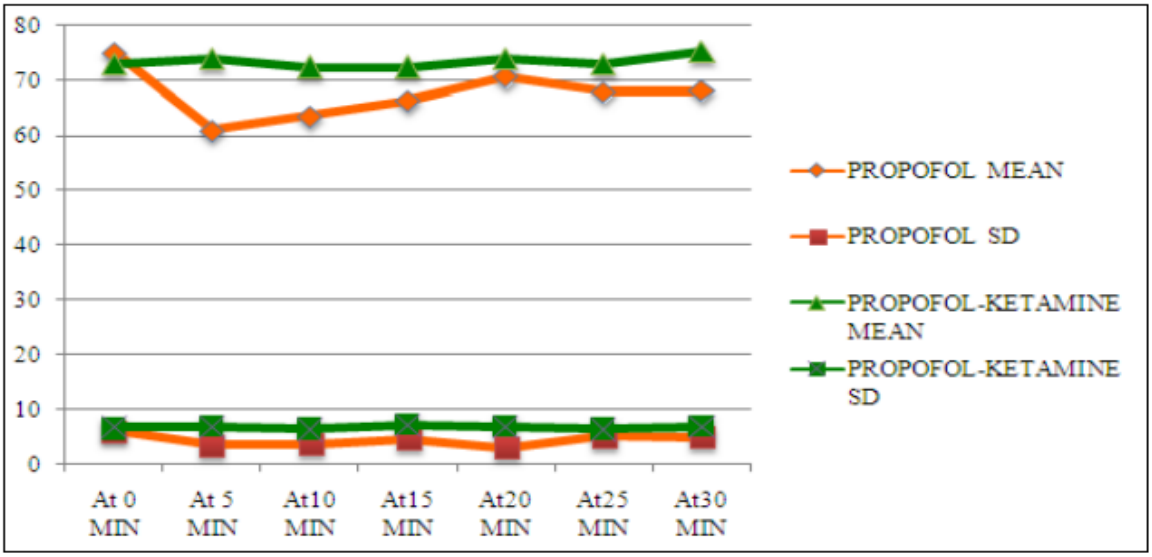

Figure 1: Intergroup comparison of changes in Diastolic blood pressure

Table 2: Intergroup comparison of changes in pulse rate

Mean PR	Propofol		Propofol-Ketamine		T stat	P Value	Inference
	Mean	SD	Mean	SD			
AT 0 MIN	79.3	5.86	77.6	4.78	1.42	>0.05	NS
AT 5 MIN	72.9	5.24	77.6	4.99	-4.06	<0.001	HS
AT 10MIN	72.2	4.87	77.5	5.10	-4.71	<0.001	HS
AT 15MIN	72.3	5.42	78.9	5.73	-5.33	<0.001	HS
AT 20MIN	72.3	5.16	77.4	5.29	-4.37	<0.001	HS
AT 25MIN	72.7	4.89	80.0	6.04	-5.98	<0.001	HS
AT 30MIN	73.1	4.92	78.6	5.49	-4.68	<0.001	HS

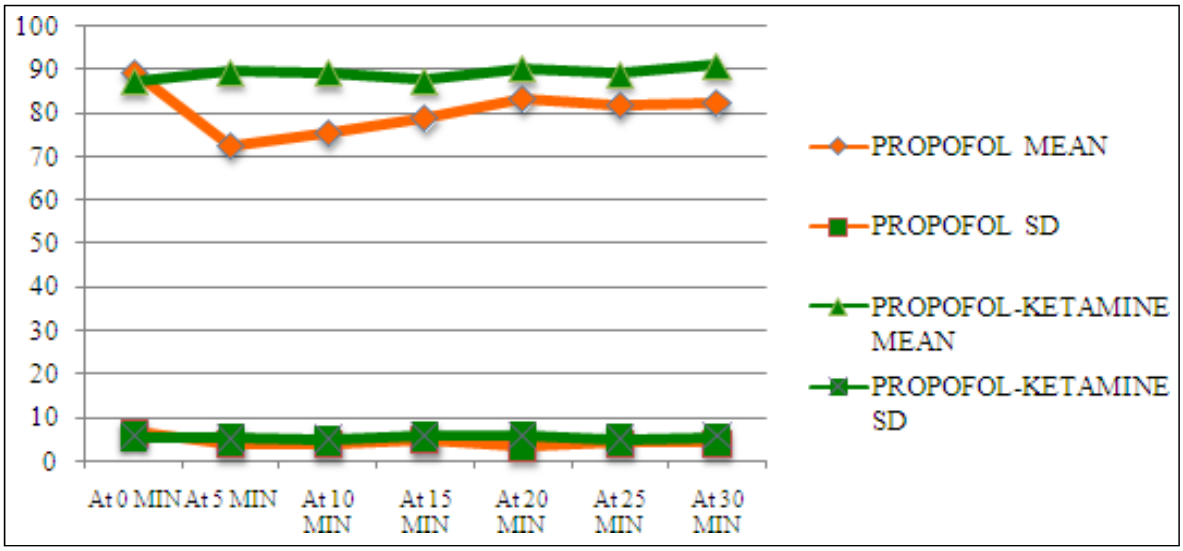

Figure 2: Intergroup comparison of changes in Mean arterial pressure

Discussion: The utilisation of total intravenous anaesthesia (TIVA) has garnered significant attention among anaesthesiologists due to its remarkable efficacy in mitigating operation room contamination. With the advent of the continuous infusion system, Total Intravenous Anaesthesia (TIVA) has garnered significant recognition in the medical field. However, it remains a challenge to find a singular intravenous (IV) medication that fulfils all the essential criteria of anaesthesia, encompassing insensibility, analgesia, and muscle relaxation. Hence, it is imperative to administer multiple therapeutic agents in order to attain the desired outcomes. When administered in subanesthetic doses, ketamine exhibits a reduction in the quantity of propofol necessary for induction. This phenomenon is commonly known as co-induction in medical and academic literature. It confers stability to the hemodynamic parameters.

In contrast to fentanyl, a study conducted by Kaushik Saha et al. [11] revealed a statistically significant reduction in the induction dosage of propofol when administered in conjunction with ketamine. In our research, the propofol induction dosage was correspondingly decreased in the group that received the propofol-ketamine combination. In a study conducted by Briggs et al. [12], utilising different concentrations of propofol (1-3mg/kg) as the primary agent for brief surgical interventions, it was ascertained that not all patients achieved anaesthesia with a dosage of 1.75 mg/kg, and that an induction dose of 2 mg/kg was deemed sufficient. The majority of patients exhibited prompt recovery, with no discernible presence of emetic sequelae. In line with the research conducted by Briggs et al. [12], our study revealed that the average dosage of propofol required for induction in the group receiving propofol alone was 2.02 0.16 mg/kg. The average induction dose of propofol in the propofol-ketamine group was determined to be 1.60 ± 0.10 mg/kg, a finding that exhibited statistical significance.

Dr. Shiba Goel and Dr. Neerja Bhardwaj, both medical doctors, carried out a research study with the aim of assessing the effectiveness of ketamine (pk) and midazolam (PM) as co-induction agents alongside propofol (P) for the purpose of laryngeal mask insertion in paediatric patients. It was observed that within group P, there was a notable reduction in systolic blood pressure compared to groups PK and PM, with statistical significance ($P<0.005$). Only 5% of patients in groups PK and PM exhibited a greater than 20% reduction in systolic blood pressure (SBP), in contrast to 89% of patients in group P ($P<0.001$). A significantly higher proportion of children in groups PK and PM were deemed appropriate candidates for LM insertion compared to those in group P ($p < 0.001$). The coadministration of propofol with ketamine or midazolam demonstrates favourable effects on hemodynamic stability and enhanced conditions for laryngeal mask insertion in paediatric patients. However, it should be noted that this approach is correlated with a prolonged recovery period. Hence, the current study was undertaken to assess the effectiveness of ketamine as a co-induction agent in conjunction with propofol compared to propofol alone.

In 2014, Martinez-Taboada and Elizabeth conducted a study [14] to evaluate the comparative efficacy of propofol and ketofol (a combination of propofol and ketamine) for inducing anaesthesia in a cohort of 70 healthy canines, subsequent to premedication. Prior to the advent of laryngoscopy and tracheal intubation techniques, the administration of either propofol (10 mg/ml) or ketofol (9 mg propofol and 9 mg ketamine/ml) was adjusted intravenously.

The volume of the induction mixture (mean ± standard deviation) was found to be

significantly lower for ketofol (0.20.1 ml/kg) compared to propofol (0.40.1 ml/kg) ($p<0.001$). The pulse rate (PR) exhibited a significant increase following the administration of ketofol (mean increase of 35 ± 20 beats per minute), whereas the effect of propofol on PR was not consistently observed (mean increase of 4 ± 16 beats per minute) ($p<0.001$). The administration of Ketofol was found to be correlated with a statistically significant increase in the mean arterial blood pressure (MAP) (82 ± 10 mmHg) compared to propofol (77 ± 11) ($p=0.05$). The administration of Ketofol resulted in a more significant reduction in FR-1 (median range) compared to propofol: Ketofol-32 (-158 to 0) versus propofol -24 (-187 to 2) respiration minute ($p<0.001$). The level of anaesthesia exhibited similar characteristics among all study cohorts.

The study findings indicate that Ketofol demonstrated a higher level of efficacy compared to propofol in the context of tracheal intubation and induction ($p=0.04$ and 0.02, respectively). The study conducted by Fernando SF Cruz et al [15] aimed to assess the efficacy of total intravenous anaesthesia (TIVA) using propofol (P) as a standalone agent or in combination with ketamine (PK) in rabbits undergoing surgical procedures.

It has been determined that the administration of ketamine in rabbits augments the anaesthetic effects induced by propofol, thereby leading to enhanced maintenance of heart rate. The study conducted by M. Koch et al. [16] aimed to assess the impact of propofol on the microcirculation of human subjects. The study sample consisted of 15 participants, with a mean age of 35 years (range: 25-41 years). During the assessment of microcirculation, the average calculated propofol effect-site concentration was 6.5 μg/mL (range: 4.5-10 μg/mL). There were no statistically significant changes observed in heart rate or peripheral capillary oxygen saturation (SpO2) throughout the anaesthesia period. However, body temperature exhibited a decrease, and arterial pressure showed a decline at the conclusion of the intervention.

In their study, Guit et al. [17] determined that the administration of propofol and ketamine in combination resulted in a state of hemodynamically stable anaesthesia, obviating the requirement for supplementary analgesic agents. All patients demonstrated typical postoperative behaviour, and none reported experiencing hallucinations during or following the surgical procedure. It has been observed that propofol demonstrates efficacy in mitigating the untoward consequences associated with a subanaesthetic dosage of ketamine in human subjects.

In our research, the group administered with propofol exhibited a statistically significant decrease in the average heart rate, average systolic blood pressure, average diastolic blood pressure, and average arterial pressure compared to the group receiving a combination of propofol and ketamine. For instance, the group administered with propofol alone exhibited a mean systolic blood pressure of 118.4 ± 9.36, while the group receiving propofol-ketamine combination displayed a mean systolic blood pressure of 117.9 ± 8.77.

These values were found to be statistically similar. In the group administered propofol alone, a significant reduction in systolic blood pressure was observed at the 5-minute mark following induction (96.3 ± 7.35). This reduction remained significant when compared to the group receiving a combination of propofol and ketamine during the entire 30-minute observation period. Comparable reductions in average diastolic blood pressure were noted in the propofol monotherapy cohort relative to the baseline average diastolic blood pressure (75.1 ± 6.14), with the most substantial decline observed at the 5-minute mark following induction (60.9 ± 3.54). During

the 30-minute period of observation, a statistically significant disparity was observed between the two groups.

A statistically significant reduction in mean arterial pressure was also observed in the group receiving propofol alone, as compared to the group receiving propofol in combination with ketamine.

Conclusion

The findings of our research indicate that the utilisation of the propofol and ketamine (PK) combination exhibits superiority over the use of propofol (P) alone in relation to maintaining haemodynamic stability.

This superiority is attributed to the reduced amount of propofol required for induction, the decreased occurrence of adverse effects, and the provision of prolonged post-operative pain relief. In the propofol-ketamine cohort, the duration of recovery from the administered induction dose was observed to be prolonged.

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